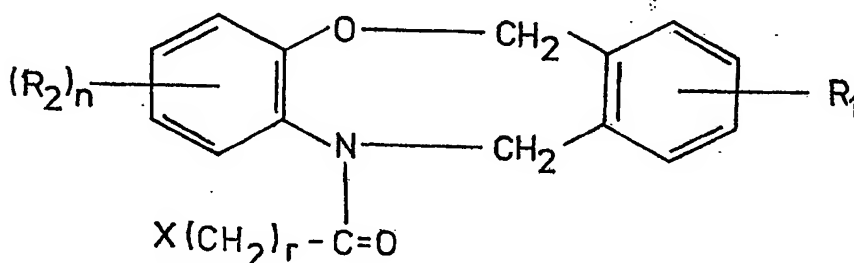


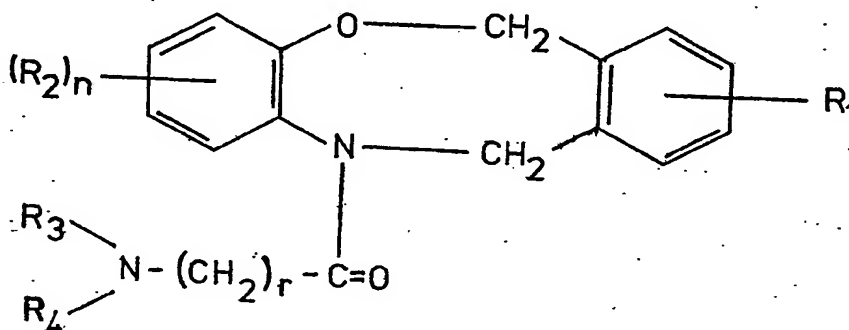
in an aprotic solvent, such as xylene, toluene, or benzene, to give a compound of the formula

(VII)



and the latter treated with ammonia or an appropriate amine to give a compound of the formula

(VIII)

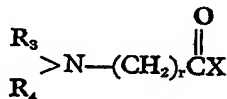


which in turn is reacted with sodium borohydride or lithium aluminum hydride in an aprotic solvent such as dioxane, diethyleneglycol, dimethyl ether, diethyl ether, or tetrahydrofuran to give a compound of formula I where lower alkylene is  $-(CH_2)_m-$ .

(4) A compound of formula (VII) where  $r$  is 1, 2 or 3 is reacted with sodium borohydride or lithium aluminum hydride in an aprotic solvent such as diethyl ether, dioxane, or tetrahydrofuran to give a compound of formula VI which is reacted with ammonia or an appropriate amine to give a compound of formula I where lower alkylene is  $-(CH_2)_m-$ ,  $m$  being 2, 3 or 4.

(5) A compound of formula IV may be reacted with an aminoacyl halide of the formula

(IX)



where  $r$  is 1, 2 or 3 and each  $X$  is chlorine or bromine to give a compound of formula VIII and the latter is reduced as in Method 3 to give a compound of formula I wherein lower alkylene is  $-(CH_2)_m$ ,  $m$  being 2, 3, or 4, which may be converted if desired into an acid addition salt.

The starting materials of formula II are produced by first reacting an unsubstituted or  $R_1$ -substituted  $o$ -halomethylbenzoic acid alkyl ester with an alkali metal salt of an unsubstituted or  $(R_2)_n$ -substituted  $o$ -nitrophenol in an organic solvent such as  $N,N$ -dimethylformamide. The resulting alkyl  $o$ -[ $o$ -nitrophenoxy]-methylbenzoate is hydrolyzed to obtain the corresponding benzoic acid. The nitro group of the latter is reduced to an amino group. This product is cyclized, for example, with  $N,N'$ -dicyclohexylcarbodiimide in ethyl acetate, to obtain a ring substituted or unsubstituted 6*H*-dibenz[*b,f*][1,4]oxazocin-11-(12*H*)one, the anion of which is reacted with an

alkylaminoalkylene halide in toluene to give the starting material of formula II; or the ring substituted or unsubstituted 6*H*-dibenz[b,f][1,4]oxazocin-11(12*H*)-one may be reduced with sodium borohydride in methanol or lithium aluminum hydride in diethylether or tetrahydrofuran to give the starting material of formula IV.

The following examples are illustrative of the invention. Temperatures are on the centigrade scale.

#### EXAMPLE 1

12-[2-(Dimethylamino)ethyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine maleate  
(a) To 103 g. of sodium *o*-nitrophenolate, 103 g. of sodium bromide, and 1100 ml. of *N,N*-dimethylformamide is added dropwise 186 g. of methyl 2-chloromethylbenzoate in 450 ml. of *N,N*-dimethylformamide, and the mixture heated about three hours at 85—90° to give about 147 g. of methyl *o*-[*o*-nitrophenoxymethyl]benzoate, m.p. about 109—111°.

(b) The product from (a), 144 g. suspended in 3600 ml. of 95% ethanol is stirred and refluxed for 10 minutes and then 31 g. of sodium hydroxide in 750 ml. of water is added as rapidly as possible. The refluxing is continued for an additional 10 minutes, the source of heat removed, and 92 ml. of concentrated hydrochloric acid in 750 ml. of water is added rapidly with vigorous stirring followed by 2100 ml. of water. The mixture is stirred, cooled, and the solid filtered to give about 126 g. of *o*-[*o*-nitrophenoxymethyl]benzoic acid, m.p. about 196—198°.

(c) The product from (b), 27 g., 200 ml. of 0.5 N sodium hydroxide and 2.0 g. Raney nickel catalyst are stirred for 10 minutes under nitrogen, and filtered. To the filtrate is added 10 g. of Raney nickel catalyst and the mixture hydrogenated at 50 p.s.i. for three hours to give about 22 g. of *o*-[*o*-aminophenoxymethyl]benzoic acid, m.p. about 178—179°.

(d) The product from (c), 8.0 g., in 750 ml. of anhydrous ethyl acetate is cooled to 18°, 7.2 g. of *N,N'*-dicyclohexylcarbodiimide in 50 ml. of anhydrous ethyl acetate is added, and the mixture stirred for 24 hours to give about 2.7 g. of 6*H*-dibenz[b,f][1,4]oxazocin-11(12*H*)-one.

(e) The product from (d), 4.9 g., in 30 ml. of *N,N*-dimethylformamide is added dropwise to a stirred suspension of 1.2 g. of 50% sodium hydride in oil dispersion at room temperature, in an atmosphere of nitrogen. During the addition the reaction temperature rises spontaneously to 35°. The resulting colorless solution is stirred at room temperature for 30 minutes, then warmed to 85°, cooled to 28°, and a solution of 4.5 g. of 2-dimethylaminoethyl bromide in 30 ml. of toluene is added dropwise. After the addition the reaction mixture is stirred at room temperature for 1 hour, then at 85°, filtered and the filtrate concentrated to give 11 g. of residue. The residue is dissolved in 350 ml. of ether and the ether solution is extracted with a solution of 3 ml. of concentrated (37%) HCl in 25 ml. of water. The aqueous acidic solution is cooled, layered with 300 ml. of ether and neutralized to a pH 11 with solid potassium carbonate. The ethereal solution of the base is separated, dried and the ether removed leaving 4.0 g. of solid, m.p. 102—104°. It is recrystallized from 35 ml. of ligroin to give about 3.0 g. of 12-[2-(dimethylamino)ethyl]-6*H*-dibenz[b,f][1,4]-oxazocin-11(12*H*)-one, m.p. about 105—106°.

(f) The product from (e) 7.6 g., in 500 ml. of anhydrous ether is added in 1 hour in an atmosphere of nitrogen to a stirred slurry of 2.7 g. of lithium aluminum hydride in 100 ml. of dry ether. Following the addition, the reaction is refluxed for 12 hours. The dropwise addition of 6 ml. of water is followed by 9 ml. of 10% sodium hydroxide and filtration from inorganic salts, then the ether is extracted with 100 ml. of 1.5% hydrochloric acid. The aqueous phase is separated, cooled, and solid potassium carbonate is added to a pH of 10.8. The base is extracted into ether and the ether solution is dried. Removal of the ether gives a yield of about 3.7 g. of 12-[2-(dimethylamino)ethyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine, as a viscous oil.

(g) To the product from (f), 3.5 g., in 10 ml. of acetone is added 2.4 g. of maleic acid in 12 ml. of acetone. The resulting solution is filtered and 15 ml. of anhydrous ether is added. The salt is recrystallized from 25 ml. of 2-propanol to give about 1.1 g. of maleate, m.p. about 155—157°.

## EXAMPLE 2

12-[3-(Diethylamino)propyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine hydrochloride

(a) Employing the procedure of Example 1(e) but substituting 3-diethylamino-propyl chloride for the 2-dimethylaminoethyl bromide, there is obtained 12-[3-diethylamino]propyl]-6H-dibenz[b,f][1,4]oxazocin-11(12H)-one, m.p. about 67—68° after recrystallization from pentane.

(b) Employing the procedure of Example 1 (f) but substituting the product from (a) for the product from Example 1 (e) there is obtained 12-[3-(diethylamino)propyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine.

(c) A solution of 4.2 g. of the product from (b) in 200 ml. of anhydrous ether is cooled in an ice-water bath and 5.0 ml. of 2.6 N ethereal hydrogen chloride is added, with stirring. The hydrochloride separates from solution and is isolated by filtration.

## EXAMPLE 3

12-[2-(Diethylamino)ethyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocin oxalate

(a) Employing the procedure of Example 1 (e) but substituting 2-diethylamino-ethyl chloride for the 2-dimethylaminoethyl bromide, there is obtained 12-[2-(diethylamino)ethyl]-6H-dibenz[b,f][1,4]oxazocin-11(12H)-one, m.p. about 70—72° after recrystallization from petroleum ether (b.p. 20—60°).

(b) Employing the procedure of Example 1(f) but substituting the product from (a) for the product from Example 1 (e) there is obtained 12-[2-(diethylamino)ethyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine.

(c) A solution of 1.1 g. of oxalic acid in 30 ml. of diisopropyl ether is added to a solution of 3.7 g. of the product from (b) in 200 ml. of diisopropyl ether. The oxalate salt separates from solution and is recovered by filtration.

## EXAMPLE 4

12-[3-(Dimethylamino)propyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine

(a) A solution of 5.0 g. of *n*-butyllithium in 50 ml. of dry hexane is added to a suspension of 11.3 g. of 6H-dibenz[b,f][1,4]oxazocin-11(12H)-one in 500 ml. of dry toluene, the whole is stirred for 1 hour at 70°, cooled to 30° and 10.0 g. of 3-dimethylaminopropyl bromide in 100 ml. of dry toluene is added dropwise. The mixture is then heated for 16 hours at 85—90° to give about 4.9 g. of 12-[3-(dimethylamino)-propyl]-6H-dibenz[b,f][1,4]oxazocin-11(12H)-one, m.p. about 98—99°, after recrystallization from hexane.

(b) Employing the procedure of Example 1 (f) but substituting the product from (a) for the product from Example 1 (e) there is obtained 12-[3-(dimethylamino)-propyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine.

## EXAMPLE 5

11,12-Dihydro-12[2-(1-pyrrolidino)ethyl]-6H-dibenz[b,f][1,4]oxazocine

(a) 11,12-Dihydro-6H-dibenz[b,f][1,4]oxazocine

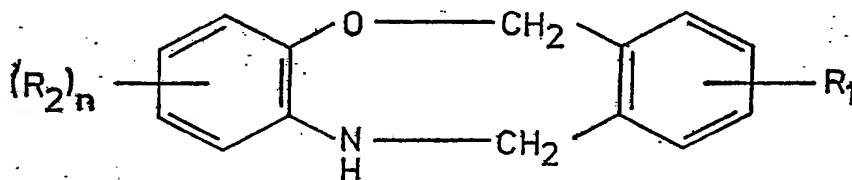
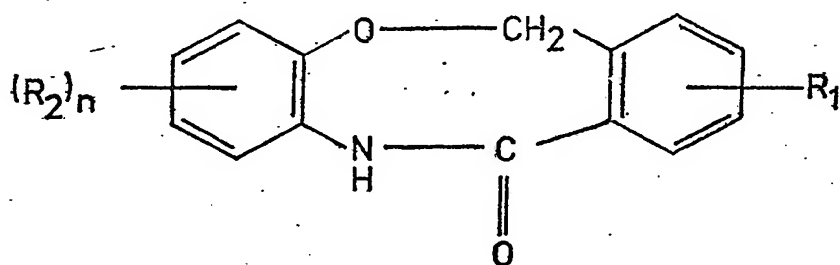
A suspension of 4.8 g. of lithium aluminum hydride in 1200 ml. of ether is stirred under nitrogen and 6.6 g. of 6H-dibenz[b,f][1,4]oxazocine-11(12H)-one is added in 1 hour. The reaction mixture is refluxed for one hour, cooled, and 10 ml. of water is added dropwise followed by 20 ml. of 10% sodium hydroxide. The inorganic solids are removed by filtration and the ethereal filtrate is dried and concentrated to give about 6 g. of solid, m.p. about 132—135°. Recrystallization from 120 ml. of cyclohexane gives about 5 g. of product, m.p. about 133—135°.

(b) A solution of 1.7 g. of *n*-butyllithium in 16 ml. of dry hexane is added to 5.2 g. of 11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine in 250 ml. of dry toluene, the whole is stirred for 16 hours and 3.6 g. of N-(2-chloroethyl)pyrrolidine in 10 ml. of dry toluene is added. The mixture is then heated for 3 hours at 90—95°, cooled, washed with water, dried and concentrated. The residue is extracted with 150 ml. of 1% hydrochloric acid. The acidic solution is adjusted to pH 11.5, the base is extracted into ether, and the dried ether solution is concentrated to give 11,12-dihydro-12-[2-(1-pyrrolidino)ethyl]-6H-dibenz[b,f][1,4]-oxazocine.

## EXAMPLE 6

By applying the procedure of Example 5 (a) to the ring substituted 6H-dibenz[b,f][1,4]oxazocine-11(12H)-one shown in the left hand part of the following table, the 11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine indicated in the right hand part of the table is obtained. Then by continuing as in 5(b) but utilizing dimethylaminoethyl bromide, the 12-dimethylaminoethyl derivative of the oxazocine is obtained.

TABLE I



| R <sub>1</sub> | R <sub>2</sub>                                     | n | R <sub>1</sub> | R <sub>2</sub>                                     | n |
|----------------|--|---|----------------|--|---|
| H              | 2-CH <sub>3</sub>                                  | 1 | H              | 2-CH <sub>3</sub>                                  | 1 |
| H              | 2-CH <sub>3</sub> O                                | 1 | H              | 2-CH <sub>3</sub> O                                | 1 |
| H              | 3-CH <sub>3</sub>                                  | 1 | H              | 3-CH <sub>3</sub>                                  | 1 |
| H              | 2-CF <sub>3</sub>                                  | 1 | H              | 2-CF <sub>3</sub>                                  | 1 |
| H              | 2-SO <sub>2</sub> N(CH <sub>3</sub> ) <sub>2</sub> | 1 | H              | 2-SO <sub>2</sub> N(CH <sub>3</sub> ) <sub>2</sub> | 1 |
| H              | 2-CH <sub>3</sub> C(=O)                            | 1 | H              | 2-CH <sub>3</sub> C(=O)                            | 1 |
| 7-Cl           | H  | 1 | 7-Cl           | H  | 1 |
| H              | 1,3-CH <sub>3</sub> O                              | 1 | H              | 1,3-CH <sub>3</sub> O                              | 1 |
| 7-Cl           | 2-CH <sub>3</sub>                                  | 1 | 7-Cl           | 2-CH <sub>3</sub>                                  | 1 |

## EXAMPLE 7

12-[2-Diisopropylamino)ethyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine  
 (a) 12-(chloroacetyl)-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine

A solution of 8.5 g. of chloroacetyl chloride in 50 ml. of toluene is added dropwise, with stirring, to 9.0 g. of 11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine and 9.0 g. of triethylamine in 400 ml. of anhydrous toluene at 5°. Following the addition, the reaction mixture is stirred at room temperature for 2 hours, filtered, and the filtrate is concentrated. The residue is recrystallized from ligroin to give about 8.5 g. of product, m.p. about 123—124°.

(b) A solution of 4.0 g. of the product from (a) in 50 ml. of benzene is added to a solution of 5.0 g. of diisopropylamine in 50 ml. of benzene and heated at reflux temperature for 2 hours. After cooling, the mixture is filtered and the filtrate concentrated. The residue is dissolved in ether and extracted with 100 ml. of 2% hydrochloric acid. The acidic solution is adjusted to pH 11.5 with 20% sodium hydroxide. The base is extracted into ether, the ether solution is dried and concentrated. The residue is recrystallized from hexane to give 12-[(diisopropylamino)acetyl]-11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine.

(c) A solution of 6.0 g. of the product from (b) in 100 ml. of anhydrous ether is added, with stirring under nitrogen, to a suspension of 1.7 g. of lithium aluminum hydride in 500 ml. of anhydrous ether. The reaction mixture is stirred for 8 hours at room temperature, 2.5 ml. of water and 5 ml. of 20% sodium hydroxide are added and the ether solution is separated from the inorganic solids. The desired 12-[2-(diisopropylamino)ethyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine is recovered by acid extraction as in Example 1 (f).

#### EXAMPLE 8

12-[3-[bis-(2-hydroxy-1-methylethyl)amino]-propyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine

(a) By substituting 10.6 g. of 3-chloropropionyl chloride for the chloroacetyl chloride in Example 7 (a) there is obtained 12-(3-chloropropionyl)-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

(b) By employing the procedure of Example 7 (b) but substituting 6.0 g. of the product from (a) for the product of 7(a) and 6.0 g. of bis-(2-hydroxy-1-methylethyl)amine for the diisopropylamine there is obtained 12-[3-[bis-(2-hydroxy-1-methylethyl)amino]propionyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

(c) By employing the procedure of Example 7 (c) but substituting the product from (b) for the product from Example 7 (b) there is obtained 12-[3-[bis-(2-hydroxy-1-methylethyl)amino]propyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

#### EXAMPLE 9

12-[3-(4-hydroxypiperidino)propyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine

(a) By employing the procedure of Example 7 (c) but substituting 5.0 g. of the product from Example 8 (a) for the product from Example 7 (b) there is obtained 12-(3-chloropropyl)-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

(b) When 8.0 g. of the product from (a), 250 ml. of ethyl methyl ketone, 4.5 g. of sodium iodide, and 6.0 g. of 4-hydroxypiperidine, are stirred and heated under reflux for 18 hours there is recovered by acid extraction 12-[3-(4-hydroxypiperidino)propyl]-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

#### EXAMPLE 10

12-[2-[2-[N-Methyl-N-(2-hydroxyethyl)]amino]ethyl]-6*H*-dibenz[b,f][1,4]-oxazocine

(a) By treating the anion from 5.2 g. of 11,12-dihydro-6*H*-dibenz[b,f][1,4]-oxazocine, prepared as in the procedure of Example 5 (b), in 250 ml. of toluene, with 6.3 g. of ethylene chlorobromide and the mixture heated one hour at 85° there is obtained 12-(2-chloroethyl)-11,12-dihydro-6*H*-dibenz[b,f][1,4]oxazocine.

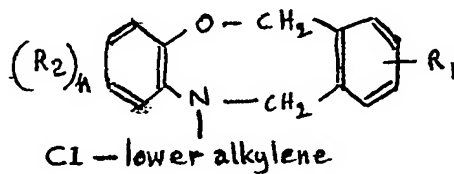
(b) By employing the procedure of 9(b) but substituting 7.6 g. of the product from (a) above for the product from 9 (a) and 5.0 g. of 2-(methylamino)ethanol, instead of the 4-hydroxy-piperidine, there is obtained 12-[2-[2-[N-methyl-N-(2-hydroxyethyl)]amino]ethyl]-6*H*-dibenz[b,f][1,4]oxazocine.

#### EXAMPLE 11

(a) By preparing the 12-haloalkylene ring substituted 6*H*-dibenz[b,f][1,4]-oxazocine shown in the left hand part of the following table by the procedure of Example 10 (a), then reacting this product as in Example 10 (b) with the amine following it in the table, the product shown in the right hand part of the following table is obtained.

TABLE

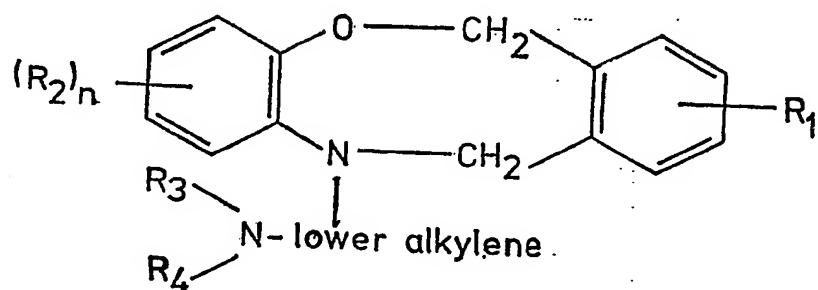
## Starting Material



| R <sub>1</sub> | R <sub>2</sub>         | n | alkylene group                  | amine   |
|----------------|------------------------|---|---------------------------------|---|
| 9-Br           | 2-Br                   | 1 | (CH <sub>2</sub> ) <sub>3</sub> | HN(CH <sub>2</sub> CH <sub>2</sub> OH) <sub>2</sub> |
| 9-F            | 2-F                    | 1 | (CH <sub>2</sub> ) <sub>2</sub> |   |
| H              | 1,2,3,4-F <sub>4</sub> | 4 | (CH <sub>2</sub> ) <sub>3</sub> |   |
| H              | 2-CH <sub>3</sub>      | 1 | (CH <sub>2</sub> ) <sub>5</sub> |   |
| H              | 2-CF <sub>3</sub>      | 1 | (CH <sub>2</sub> ) <sub>3</sub> |   |
| H              | 2-CF <sub>3</sub>      | 1 | (CH <sub>2</sub> ) <sub>3</sub> |   |
| H              | H                      | 1 | (CH <sub>2</sub> ) <sub>2</sub> |   |

## II

Product



| R <sub>1</sub> | R <sub>2</sub>         | n | substituent in 12-position |
|----------------|------------------------|---|----------------------------|
| 9-Br           | 2-Br                   | 1 | $-(CH_2)_3N(CH_2CH_2OH)_2$ |
| 9-F            | 2-F                    | 1 |                            |
| H              | 1,2,3,4-F <sub>4</sub> | 4 |                            |
| H              | 2-CH <sub>3</sub>      | 1 |                            |
| H              | 2-CF <sub>3</sub>      | 1 |                            |
| H              | 2-CF <sub>3</sub>      | 1 |                            |
| H              | H                      | 1 |                            |

TABLE II

| $R_1$ | $R_2$  | $n$ | alkylene group  | amine  |
|-------|--|-----|---|--|
| H     | 2-CF <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>2</sub>                           | NH <sub>2</sub> CH <sub>3</sub>  |
| H     | 2-CF <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | NH <sub>3</sub>  |
| H     | 2,3-CH <sub>3</sub>                                | 2   | CH <sub>2</sub> CHCH <sub>2</sub><br> <br>CH <sub>3</sub> | HN(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>  |
| H     | 2-CF <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{CHOH} \\ \text{CH}_2-\text{CH}_2 \end{array}$   |
| H     | 2-CF <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{CHCH}_2\text{NH}_2 \\ \text{CH}_2-\text{CH}_2 \end{array}$  |
| H     | 2-CH <sub>3</sub> O                                | 1   | (CH <sub>2</sub> ) <sub>2</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{S} \\ \text{CH}_2-\text{CH}_2 \end{array}$  |
| H     | 2-(CH <sub>3</sub> ) <sub>2</sub> NSO <sub>2</sub> | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_3 \\   \\ \text{CH}-\text{CH}_2 \\ \text{HN} \quad \quad \text{CH}_2 \\   \\ \text{CH}-\text{CH}_2 \\   \\ \text{CH}_3 \end{array}$                        |
| H     | 2-CH <sub>3</sub> C(=O)                            | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{NCH}_2\text{CH}_2\text{OH} \\ \text{CH}_2-\text{CH}_2 \end{array}$                                |
| 7-Cl  | 2-CH <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{N}-\text{C}(=\text{O})-\text{OCH}_3 \\ \text{CH}_2-\text{CH}_2 \end{array}$                                   |
| H     | 2-CF <sub>3</sub>                                  | 1   | (CH <sub>2</sub> ) <sub>3</sub>                           | $\begin{array}{c} \text{CH}_2-\text{CH}_2 \\ \text{HN} \quad \quad \text{N}-\text{CH}_2\text{CH}_2\text{OC}(=\text{O})-\text{C}_6\text{H}_{13} \\ \text{CH}_2-\text{CH}_2 \end{array}$ |



Continued

| $R_1$ | $R_2$  | n | substituent in 12-position  |
|-------|--|---|---|
| H     | 2-CF <sub>3</sub>  | 1 | -(CH <sub>2</sub> ) <sub>2</sub> NHCH <sub>3</sub>  |
| H     | 2-CF <sub>3</sub>  | 1 | -(CH <sub>2</sub> ) <sub>3</sub> NH <sub>2</sub>  |
| H     | 2,3-CH <sub>3</sub>  | 2 | $\begin{array}{c} \text{---CH}_2\text{CHCH}_2\text{N}(\text{C}_2\text{H}_5)_2 \\   \\ \text{CH}_3 \end{array}$  |
| H     | 2-CF <sub>3</sub>  | 1 | $\begin{array}{c} \text{CH}_2\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_3\text{N} \qquad \text{CHOH} \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$  |
| H     | 2-CF <sub>3</sub>  | 1 | $\begin{array}{c} \text{CH}_2\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_3\text{N} \qquad \text{CHCH}_2\text{NH}_2 \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$   |
| H     | 2-CH <sub>3</sub> O  | 1 | $\begin{array}{c} \text{CH}_2\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_2\text{N} \qquad \text{S} \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$   |
| H     | 2-(CH <sub>3</sub> ) <sub>2</sub> NSO <sub>2</sub>                       | 1 | $\begin{array}{c} \text{CH}_3 \\   \\ \text{CH---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_4\text{N} \qquad \text{CH}_2 \\   \qquad \qquad   \\ \text{CH---CH}_2 \\   \\ \text{CH}_3 \end{array}$  |
| H     | $\begin{array}{c} \text{O} \\    \\ 2\text{---CH}_3\text{C} \end{array}$ | 1 | $\begin{array}{c} \text{CH}_2\text{---CH}_2\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_3\text{N} \qquad \text{NCH}_2\text{CH}_2\text{OH} \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$   |
| 7-Cl  | 2-CH <sub>3</sub>  | 1 | $\begin{array}{c} \text{CH}_3\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_3\text{N} \qquad \text{N} \begin{array}{c} \text{O} \\    \end{array} \text{C---OCH}_3 \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$                                      |
| H     | 2-CF <sub>3</sub>  | 1 | $\begin{array}{c} \text{CH}_2\text{---CH}_2 \\   \qquad \qquad   \\ \text{---(CH}_2)_3\text{N} \qquad \text{N---CH}_2\text{CH}_2\text{OC} \begin{array}{c} \text{O} \\    \end{array} \text{---C}_6\text{H}_{13} \\   \qquad \qquad   \\ \text{CH}_2\text{---CH}_2 \end{array}$ |

## EXAMPLE 12

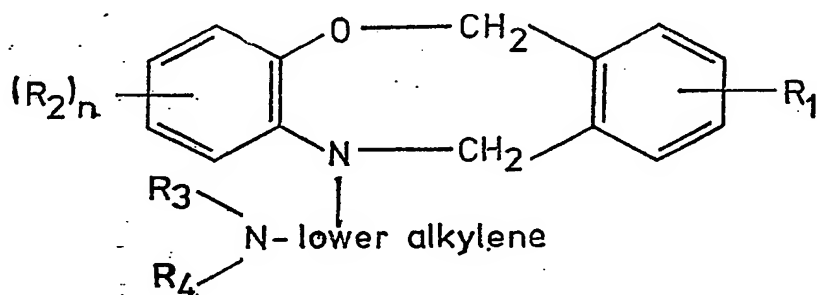
## 12-[3-(Dibutylamino)propyl]-6H-dibenz[b,f][1,4]oxazocine

(a) By employing the procedure of Example 5 (b) to prepare the anion from 10.4 g. of 11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine and 3.4 g. of n-butyllithium in 500 ml. of dry toluene but substituting 5.0 g. of 3-dibutylaminopropionyl chloride for the N-(2-chloroethyl)pyrrolidine and stirring the reaction mixture for one hour at room temperature there is obtained 12-[3-(dibutylamino)propionyl]-6H-dibenz[b,f]-[1,4]oxazocine.

(b) By employing the procedure of Example 7 (c) but substituting the product of (a) for the product from 7 (b) there is obtained 12-[3-(dibutylamino)propyl]-6H-dibenz[b,f][1,4]oxazocine.

## WHAT WE CLAIM IS:—

1. A compound of the formula



wherein the lower alkylene group has not more than 5 carbon atoms,  $R_1$  is hydrogen or halogen,  $R_2$  is hydrogen, halogen, trihalomethyl, lower alkoxy, trihalomethoxy, trihalomethylmercapto, lower alkyl, N,N-di-alkylsulfamoyl or lower alkanoyl,  $R_3$  and  $R_4$  each represent hydrogen, lower alkyl, lower alkoxy, or  $\omega$ -hydroxy-lower alkyl, or  $R_3$  and  $R_4$  together with the nitrogen atom to which they are attached form a 5- to 7-membered nitrogen heterocycle which may contain one additional oxygen, sulfur or nitrogen hetero atom in the ring, and which may be substituted with one to three of the groups represented by  $R_2$  or hydroxy-lower alkyl, hydroxy-lower alkoxy-alkyl,  $C_1-C_{14}$  alkanoyloxy-lower alkyl, carbo-lower alkoxy, or 2-( $C_1-C_{14}$  alkanoyloxy-lower alkoxy) lower alkyl, said radical, when substituted, containing less than 21 atoms, excluding hydrogen, in the radical, and  $n$  is 1 to 4 or an acid addition salt thereof.

2. A compound as claimed in Claim 1 wherein  $R_1$  and  $R_2$  are each hydrogen and  $R_3$  and  $R_4$  are each lower alkyl.

3. A compound as claimed in Claim 1 wherein  $R_1$  is hydrogen,  $R_2$  is chlorine,  $R_3$  and  $R_4$  are each lower alkyl and  $n$  is 1.

4. A compound as claimed in Claim 1 wherein  $R_1$  is hydrogen,  $R_2$  is trifluoromethyl,  $R_3$  and  $R_4$  are each lower alkyl and  $n$  is 1.

5. A compound as claimed in Claim 2 wherein each lower alkyl group is methyl and the lower alkylene group has 2 carbons.

6. A compound as claimed in claim 2 wherein each lower alkyl group is methyl and the lower alkylene group has 3 carbons.

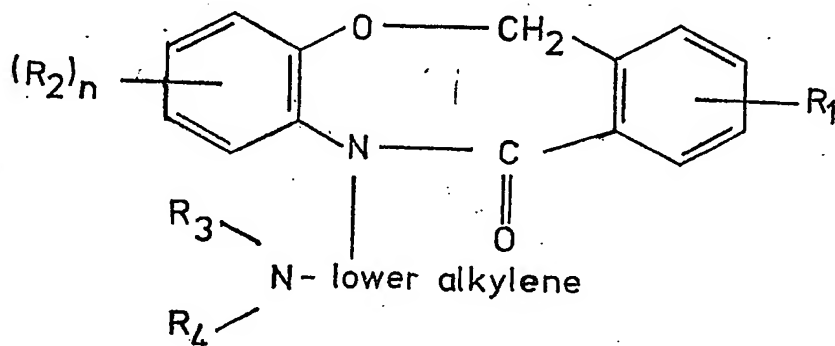
7. A compound as claimed in Claim 1, wherein  $R_1$  and  $R_2$  each is hydrogen, ( $R_3$ ) ( $R_4$ )N is hydroxyethylpiperazino and the lower alkylene group has 3 carbons.

8. A compound as claimed in Claim 1 wherein  $R_1$  and  $R_2$  each is hydrogen, ( $R_3$ ) ( $R_4$ )N is methylpiperazino and the lower alkylene group has 3 carbons.

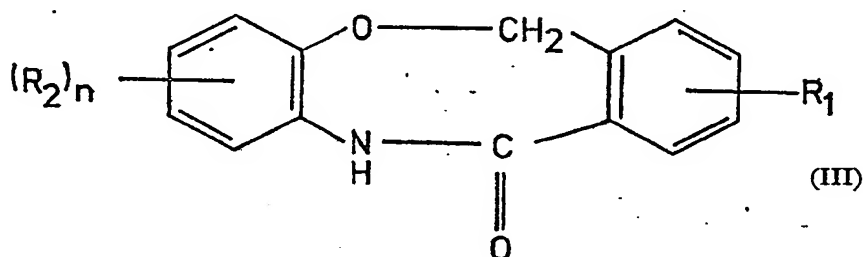
9. A compound as claimed in Claim 1 wherein  $R_1$  is hydrogen,  $R_2$  is trifluoromethyl, ( $R_3$ ) ( $R_4$ )N is hydroxyethylpiperazino, the lower alkylene group has 3 carbons and  $n$  is 1.

10. A process for preparing compounds as defined in Claim 1 and acid addition salts thereof, characterized in that:

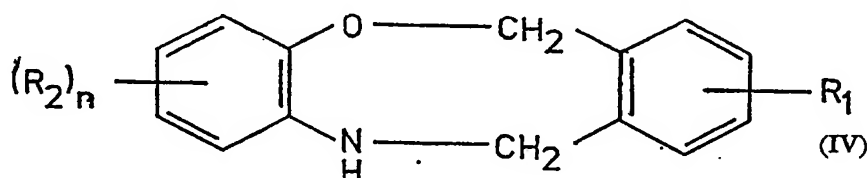
(a) a compound of the formula



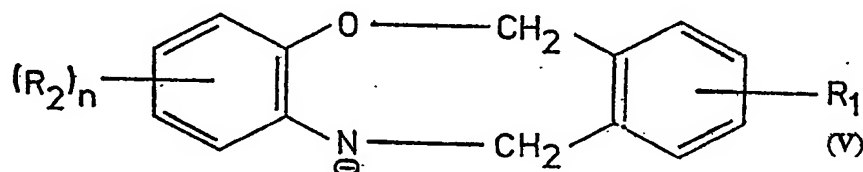
5 is treated with sodium borohydride in methanol or with lithium aluminum hydride in an aprotic solvent; or  
 (b) a compound of the formula



10 is treated with sodium borohydride in methanol or with lithium aluminum hydride in an aprotic solvent to give a compound of the formula



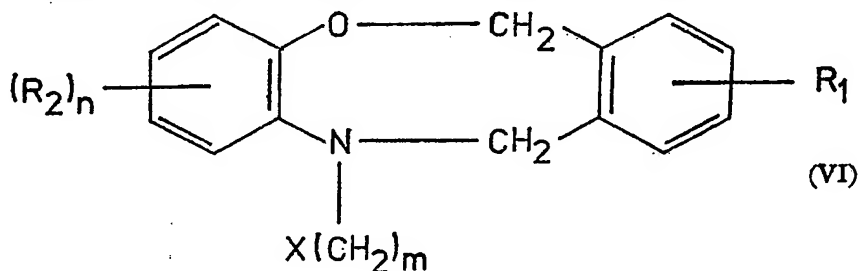
which is reacted with an alkali or alkaline earth metal hydride, or a metal alkyl derivative, in an aprotic solvent, or a mixture of aprotic solvents, to form the anion



15 which is then treated with an appropriate aminoalkyl halide, to give a compound of which is then treated with an appropriate aminoalkyl halide, to give a compound of structure (I), or is treated with a haloalkylene halide of the formula  $X(CH_2)_mX$  where

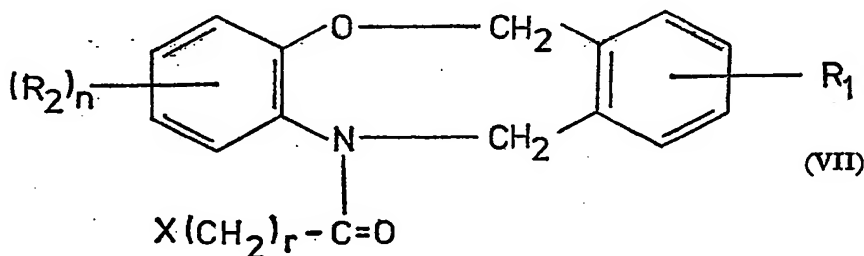
15

each X is chlorine or bromine and  $m$  is 2, 3 or 4 to give the 12-haloalkylene derivative

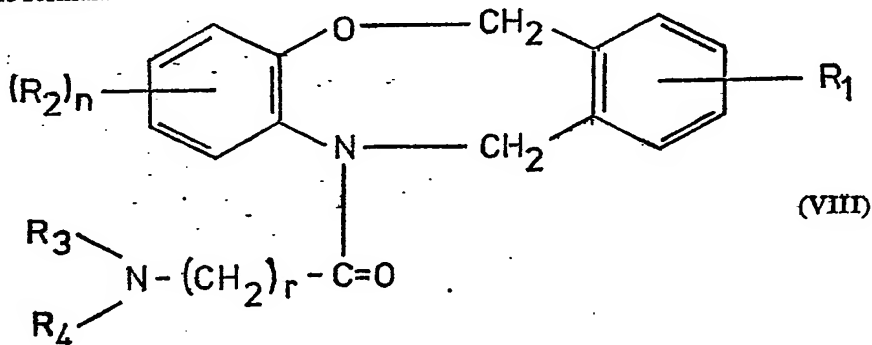


wherein X is Cl or Br and  $m$  is 2, 3 or 4 and the compound VI is treated with ammonia or an appropriate amine to give compounds of structure I in which lower alkylene is  $-(CH_2)_m-$  or

(c) a compound of formula IV is treated with a haloacyl halide of the formula  $X(CH_2)_rCOX$  where each X is chlorine or bromine and  $r$  is 1, 2 or 3 in the presence of a basic hydrohalide acceptor in an aprotic solvent to give a compound of the formula



and the latter is treated with ammonia or an appropriate amine to give a compound of the formula



which in turn is reacted with sodium borohydride or lithium aluminum hydride in an aprotic solvent to give a compound of formula I, wherein lower alkylene is  $-(CH_2)_m-$ ,  $m$  being 2, 3 or 4; or

(d) a compound of formula (VII) is reacted with sodium borohydride or lithium aluminum hydride in an aprotic solvent to give a compound of formula VI which is reacted with ammonia or an amine to give a compound of formula I, wherein lower alkylene is  $-(CH_2)_m-$ ,  $m$  being 2, 3 or 4; or

(e) a compound of formula IV is reacted with an aminoacyl halide of the formula



where X is chlorine or bromine and  $r$  is 1, 2 or 3 to give a compound of formula VIII and the latter is reduced as in (c) to give a compound of formula I, wherein lower alkylene is  $-(CH_2)_m-$ ,  $m$  being 2, 3 or 4, and the compound I produced is converted into an acid addition salt if desired.

- 5      11. 12 - [2 - (Dimethylamino)ethyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]-oxazocine maleate. 5
12. 12 - [3 - (Diethylamino)propyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]-oxazocine hydrochloride.
- 10      13. 12 - [2 - (Diethylamino)ethyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]-oxazocin oxalate. 10
14. 12 - [3 - (Dimethylamino)propyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]oxazocine.
- 15      15. 11,12-Dihydro-12[2-(1-pyrrolidino)ethyl]-6H-dibenz[b,f][1,4]oxazocine. 15
16. 12 - [2 - (Diisopropylamino)ethyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]oxazocine.
17. 12 - [3 - [bis - (2 - hydroxy - 1 - methylethyl)amino] - propyl] - 11,12-dihydro-6H-dibenz[b,f][1,4]oxazocine.
18. 12 - [3 - (4 - hydroxypiperidino)propyl] - 11,12 - dihydro - 6H - dibenz[b,f][1,4]-oxazocine.
- 20      19. 12 - [2 - [2 - [N - Methyl - N - (2 - hydroxyethyl)]amino]ethyl] - 6H-dibenz[b,f][1,4]oxazocine. 20
20. A process as claimed in claim 10 substantially as herein described.

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